MAY 0 9 2002

K020566

FUJIREBIO DIAGNOSTICS, INC.

510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: **K020566**.

Submitter Information

Address:	Fujirebio Diagnostics, Inc. 201 Great Valley Parkway Malvern, PA 19355
Contact person:	Daniel J. O'Shannessy, Ph.D., (610) 240-3811
Summary preparation date:	February 15, 2002

Name of Device

Trade/Proprietary Name:	Fujirebio Diagnostics CA 19-9™ RIA
Common/Usual Name:	Immunological test for 1116NS19-9 Antibody Defined Antigen (CA 19-9)
Classification Name:	21CFR 866.6010, Class II, Tumor Associated Antigen Immunological Test System

Predicate Device

Abbott Laboratories AxSYM® CEA MEIA

Device Description

The Fujirebio Diagnostics CA 19-9™ RIA is a solid-phase radioimmunoassay based on the forward sandwich principle. Polystyrene beads coated with a mouse monoclonal antibody against CA 19-9 are incubated with a serum or plasma specimen, or the appropriate standards or controls. During the incubation, the CA 19-9 antigen present in the specimen is specifically bound to the solid support by the mouse monoclonal antibody. Unbound material present in the specimen is removed by aspiration and washing of the beads. The same mouse monoclonal anti-CA 19-9 labeled with ^{125}I is then incubated with the beads and binds

to the CA 19-9 antigen already bound to the beads. Unbound labeled antibody is removed by aspiration and washing. The bound radioactivity is determined by counting the beads in a gamma counter. A standard curve is obtained by plotting the CA 19-9 antigen concentration of the standards *versus* bound radioactivity. The CA 19-9 antigen concentrations of unknown patient specimens are determined from the standard curve and are directly proportional to the concentration of the bound tracer molecules.

Intended Use

The Fujirebio Diagnostics CA 19-9™ RIA, an *in vitro* diagnostic test for the quantitative measurement of the CA 19-9 tumor associated antigen, in human serum or plasma, is indicated for the serial measurement of CA 19-9 to aid in the management of patients diagnosed with cancers of the exocrine pancreas. The test is useful as an aid in:

Monitoring of disease status in those patients having confirmed pancreatic cancer who have levels of serum or plasma CA 19-9 above the cutoff, at the time of diagnosis.

CA 19-9 values must be interpreted in conjunction with all other available clinical and laboratory data before a medical decision is determined.

Summary of Performance characteristics

Analytical Sensitivity (Minimal Detectable Dose)
The analytical sensitivity was determined to be 0.9 U/mL. This level of analytical sensitivity is well below the established "cut-off" of 37 U/mL.

Interfering Substances
The appropriate NCCLS guideline was followed to determine possible sources of interference with the Fujirebio Diagnostics CA 19-9™ RIA kit. Only human anti-mouse antibodies (HAMA), at a titer of 16,636, showed potential interference with the assay. This concentration of human anti-mouse antibody is extremely high. HAMA was also tested at a lower titer of 1664 and showed no effect on the assay. All other substances that were tested with the Fujirebio Diagnostics CA 19-9™ RIA kit showed no interference at the levels tested.

Recovery Studies
Ten (10) patient samples were spiked with purified CA 19-9 antigen at three (3) different levels. Results were reported as percent recoveries (% Recovery) and compared to the acceptable percent Recovery Limits calculated using the precision of the assay diluent buffer (which was run as samples, both spiked and unspiked).

For the Low spike samples, where the values of added antigen were approximately 8 U/mL, acceptable limits of % Recovery were calculated as being 87.9 – 112.1%. For the Mid spike samples, where the values of added antigen were approximately 29 U/mL, acceptable limits of % Recovery were calculated to be 81.9 – 118%. For the High spike samples, where the values of added antigen were approximately 90 U/mL, acceptable limits of % Recovery were calculated to be 93.0 – 107.0%. These data are listed in the table below.

Patient Number	Low Spike Percent Recovery	Mid – Spike Percent Recovery	High Spike Percent Recovery
1	110.23%	103.42%	111.58%
2	112.12%	101.87%	96.49%
3	114.08%	102.35%	99.07%
4	121.37%	102.30%	107.50%
5	112.41%	102.89%	100.45%
6	92.31%	102.18%	99.99%
7	117.43%	100.93%	98.81%
8	101.98%	97.75%	99.10%
9	99.64%	102.43%	98.49%
10	101.78%	102.96%	99.78%
Mean	**108.34%**	**101.91%**	**101.13%**

Linearity

The linearity of the Fujirebio Diagnostics CA 19-9 RIA was tested with serial dilutions of 12 individuals with elevated CA 19-9 assay values. Dilutions were prepared in CA 19-9 0 Standard/Diluent. Regression analysis comparing observed and expected CA 19-9 assay values yielded a mean slope for the twelve samples of 0.96 ± 0.031 and a mean y-intercept of 5.97 ± 7.65.

Reproducibility:

Each of three (3) sites performed one (1) run per day for thirteen (13) acceptable days with three (3) different lots of product. Test materials were assayed in random order for each run, but were tested identically across each lot of reagent under evaluation.

The total average variability ranged from 6.7% (44 U/mL) to 15.4% (8 U/mL). Day-to-day variation across sample-site-lot combinations peaked at 14.9 % CV with a nadir of 0%. The maximum intra-assay variation was 18 % at a CA 19-9 concentration of 8 U/mL, a concentration below the first non-zero calibrator and well under the clinical cut-off of 37 U/mL. The average intra-assay variation across all sites and lots for that 8 U/mL sample was 12.5 % CV. For all other concentrations tested, the average intra-assay variation did not exceed 6.5% CV.

Clinical Data

Apparently Healthy Subjects:

To determine the distribution of CA 19-9 values in apparently normal healthy individuals, and to confirm the cutoff of 37 U/mL, a sample of 200 women and 200 men who were apparently disease free were assessed.

Fujirebio Diagnostics CA 19-9™ RIA Distribution of Values of Apparently Healthy Subjects

Group	Total	<37 U/mL	37 – 49.9 U/mL	50 – 69.9 U/mL	70 – 99.9 U/mL	≥100 U/mL
Males	200	189 (94.5%)	4 (2.0%)	5 (2.5%)	0 (0.0%)	2 (1.0%)
Females	200	186 (93.0%)	7 (3.5%)	4 (2.0%)	2 (1.0%)	1 (0.5%)

Benign Disease Cohorts:

Three hundred and ninety-nine (399) benign disease patient cohorts were assembled to determine the distribution of serum CA 19-9 values in benign diseases that may be co-existent in patients with confirmed pancreatic cancer.

Fujirebio Diagnostics CA 19-9™ RIA Distribution of Values Benign Diseases

Diagnostic Group	Total	<37 U/mL	37 – 49.9 U/mL	50 – 69.9 U/mL	70 – 99.9 U/mL	≥100 U/mL
Benign Diseases of the Genitourinary Tract	99	90 (90.9%)	6 (6.1%)	2 (2.0%)	1 (1.0%)	0 (0.0%)
Benign Diseases of the Gastrointestinal Tract	100	88 (88.0%)	7 (7.0%)	3 (3.0%)	2 (2.0%)	0 (0.0%)
Benign Diseases of the Pancreas/Pancreatitis	100	94 (94.0%)	1 (1.0%)	4 (4.0%)	1 (1.0%)	0 (0.0%)
Chronic Heart Disease/ Hypertension	100	80 (80.0%)	10 (10.0%)	5 (5.0%)	5 (5.0%)	0 (0.0%)

Monitoring of Disease Status in Patients Diagnosed with Pancreatic Cancer:

The effectiveness of CA 19-9 as an aid in monitoring of disease status in patients diagnosed with pancreatic cancer was determined by assessing changes in CA 19-9 levels in serial serum sets with changes in disease status. Samples from 61 patients with a total of 234 observations were analyzed. The average number of observations per patient was 3.84. Fifty-seven percent (57%) of the positive serum sets correlated with disease progression while seventy-one (71%) of serum sets showing no significant change in the marker correlated with no progression. The Table below presents the data in a 3x3 classification scheme.

The disease states are:

- Progression from one collection to the next collection (Progressing).
- No Change in disease status (Stable).
- Reduction in the signs and symptoms of the disease from one collection to the next (Responding).

Marker changes are classified as:

- A 20% or greater increase in the marker from one collection to the next (INC)
- No significant change in the marker (|Delta CA 19-9|<20%) (NC)
- A 20% or greater decrease in the marker value from one collection to the next (DEC)

Expanded Distribution

Marker Change	Disease Status			Total
	Progressive	Stable	Responding	
INC	31	30	4	65
	56.4% (1.29)	32.3% (.477)	16.0% (.190)	37.6%
NC	12	41	7	60
	21.8% (.279)	44.1% (.789)	28.0% (.389)	34.7%
DEC	12	22	14	48
	21.8% (.279)	23.7% (.310)	56.0% (1.27)	27.7%
Total	55	93	25	173

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 0 9 2002

Daniel J. O'Shannessy, Ph.D.
Chief Scientific Officer
Fujirebio Diagnostics, Inc.
201 Great Valley Parkway
Malvern, Pennsylvania 19355-1307

Re: k020566
Trade/Device Name: Fujirebio Diagnostics CA 19-9™ RIA
Regulation Number: 21 CFR § 866.6010
Regulation Name: Tumor Associated antigen Immunological Test System
Regulatory Class: II
Product Code: NIG
Dated: April 19, 2002
Received: April 23, 2002

Dear Dr. O'Shannessy:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): **K020566**

Device Name: Fujirebio Diagnostics CA 19-9™ RIA

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Sousan S. Altaie

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K020566

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Concurence of CDRH, Office of Device Evaulation (ODE)